

P. NOBLE JAMIESON and D. G. SHAW*
*Departments of Paediatrics and Radiology, University
 College Hospital, Gower Street, London WC1E
 6AU.*

*Correspondence to Dr. D. G. Shaw.

Levels of albumin, α -fetoprotein, and IgG in human fetal cerebrospinal fluid

The estimation of total protein and the relative concentration of specific components of the cerebrospinal fluid (CSF) have been the subject of many investigations because of their significance as diagnostic aids in various pathological conditions (Kabat, Moore, and Landow, 1942; Burtin, 1960; Laterre, Heremans and Carbonara, 1964; Davson, 1967; Laterre, 1973). Protein levels in samples of lumbar CSF from normal adults range between 20 and 40 mg/100 ml. During the first 3 months of life the total protein concentration of CSF appears to be higher, even reaching 120 mg/100 ml.

We report the results of estimating the levels of three proteins, α -fetoprotein (AFP), albumin, and IgG, in CSF from human fetuses. These studies are relevant to the question of the origin of AFP in amniotic fluids of fetuses with 'open' neural-tube defects and to the problem of the permeability of the blood-brain barrier during fetal life.

Materials and methods

Samples of CSF were obtained by aspiration with a syringe either from the lateral ventricles of the brain or from the upper cervical regions of the spinal cord. Six samples which were absolutely clear and free from contamination by blood were assayed; other samples, slightly contaminated, were discarded. 2 fetuses were fresh specimens, spontaneously aborted and apparently

normal. 4 were obtained by hysterotomy; of these, 3 had chromosome abnormalities (Down's syndrome), while the fourth was a male fetus borne by a female carrier of the gene for haemophilia. CSF from these fetuses was collected within 2-5 hours of the hysterotomy. Ages of the fetuses ranged between 16½ and 25½ weeks (Table I).

TABLE I

Age, cause of abortion, and chromosome complement of the 6 fetuses studied

Fetus	Age (w)	Causes of abortion	Chromosome complements
1	16½	Spontaneous	Not tested
2	19½	Spontaneous	Not tested
3	18	Induced	47,XY,+G
4	25	Induced	46,XY
5	25½	Induced	46,XY-G+t(DqGq)
6	25½	Induced	47,XY,+G

Albumin level was measured by the single radial diffusion technique and AFP by the one dimensional antigen-antibody electrophoresis (rocket technique), as previously described (Seller *et al.*, 1973). IgG levels were estimated using commercially available immunoplates (Behringwerke, AG, Marburg, Germany).

Results and conclusions

AFP levels in fetal CSF were found to decline from 1220 μ g/ml in the 16½-week-old fetus to 52 and 60 μ g/ml in the older fetuses tested (Table II). Reduction of the concentration of AFP in CSF, in relation to the ages of the fetuses, was more rapid than that of the levels of AFP in fetal sera. The ratios between the amounts of albumin and AFP in CSF increased with age, passing from 1.8 in a fetus 18 weeks old to 20 in a fetus 25½ weeks old.

IgG in adult CSF ranges from 20-40 μ g/ml (Davson, 1967; Laterre, 1973). It was therefore of great interest to find higher levels of IgG in the CSF of the fetuses. Since most of the IgG present

TABLE II

Levels of AFP, albumin, and IgG in CSF from 6 fetuses

Fetus	Levels of AFP (μ g/ml)			CSF levels (μ g/ml) of			
	(1) CSF	(2) Serum	1/2	(3) Alb	3/1	(4) IgG	3/4
1	1220	Not tested				Not tested	
2	1040	Not tested				Not tested	
3	420	2720	6.47	760	1.8	72	10.5
4	71	1380	11.4	840	11.8	117	7.12
5	52	840	16.4	680	13.1	60	11.3
6	60	690	11.5	1200	20.0	109	11.0

in fetal sera is derived from the maternal circulation and there is no evidence that these proteins are secreted by the choroidal plexi, it seems that IgG molecules present in fetal CSF are derived from blood. These findings support the suggestion that the permeability of the blood-brain barrier is not fully developed during fetal life (Davson, 1967).

The presence of high AFP levels in fetal CSF raises another important point in relation to the increased levels of this fetal protein in the amniotic fluids of fetuses with 'open' neural-tube defects (Brock and Sutcliffe, 1972; Seller *et al.*, 1973). It has been repeatedly suggested that in conditions where the neural tissue is exposed, AFP passes from the CSF into the amniotic cavity. The observation that AFP is present in high concentration in fetal CSF seems to support this hypothesis, though other mechanisms may be involved as well (Adinolfi, 1974).

Summary

Cerebrospinal fluid from 6 fetuses, 16½–25½ weeks of gestation, was assayed for the levels of α -fetoprotein, albumin, and IgG. All these proteins were present in significant amounts. The level of α -fetoprotein decreased, albumin increased, and IgG remained roughly constant during this period. These results suggest that the permeability of the blood-brain barrier is not fully developed in the fetus.

This work was supported by the Spastics Society and the Medical Research Council. We thank Susan Blunt, M. R. Creasy, and Dr. J. D. Singer for abortion specimens and chromosome results.

REFERENCES

- Adinolfi, M. (1975). On the transfer of alpha-fetoprotein from the fetus into the maternal circulation. *Maternofoetal Transmission of Immunoglobulins*. Proceedings of Symposium on Transmission of Plasma Proteins, Bangor, 1974. Ed. by W. H. Hemmings. Cambridge University Press, London. (In the press).
- Brock, D. J. H., and Sutcliffe, R. G. (1972). Alpha-fetoprotein in the antenatal diagnosis of anencephaly and spina bifida. *Lancet*, **2**, 197.
- Burtin, P. (1960). Les proteines du liquide cephalo-vachidien. *Analyse Immuno-electrophoretique*, p. 245. Ed. by P. Grabar and P. Burtin. Masson, Paris.
- Davson, H. (1967). *Physiology of the Cerebrospinal Fluid*. Churchill, London.
- Kabat, E. A., Moore, D. H., and Landow, H. (1942). An electrophoretic study of the protein components in cerebro-spinal fluid and their relationship to the serum proteins. *Journal of Clinical Investigation*, **21**, 571.
- Latterre, E. C. (1973). The normal protein pattern in cerebrospinal fluid. *La Ricerca in Clinica in Laboratorio*, **3**, 736.
- Latterre, E. C., Heremans, J. F., and Carbonara, A. O. (1964). Immunological comparison of some proteins found in cerebrospinal fluid, urine and extract from brain and kidney. *Clinica Chimica Acta*, **10**, 197.
- Seller, M. J., Campbell, S., Coltart, T. M., and Singer, J. D. (1973). Early termination of anencephalic pregnancy after detection by raised alpha-fetoprotein levels. *Lancet*, **2**, 73.

M. J. SELLER and M. ADINOLFI*
Paediatric Research Unit, Guy's Hospital Medical School, London SE 1 9RT.

*Correspondence to Dr. M. Adinolfi.

Children with duodenal ulcers and their families

Duodenal ulcer in children has been reported with increasing frequency in recent years (Robb, Orszulok, and Odling-Smee, 1972), but there is little information available concerning the incidence of peptic ulcer in the families of these patients with duodenal ulcer. An effort has been made in this study to determine the incidence of peptic ulcer in the relatives of affected children.

Materials and methods

Thirty-seven children were admitted with duodenal ulcer to this hospital in Dublin from 1960 to 1973. There were 24 boys and 13 girls, ages ranging from 15 months to 14 years. Diagnosis was made by barium meal examination in 34 patients, at operation in 2, and the ulcer was discovered at necropsy in one patient. A family history of peptic ulcer was recorded and was regarded as positive if one or other parent, grandparent, sib, aunt, or uncle was known to have the ulcer on the basis of barium meal examination or previous gastric surgery.

Results

The study revealed that 23 of the 37 children (62%) had a positive family history of peptic ulcer; 8 patients had a negative family history; and in 6 cases no family history could be obtained. A total of 40 relatives were found to have definite ulcers (Table). 13 children had only one relative with an ulcer. In the remaining 10 children there were 2 or more affected relatives.

Investigation of the degree of relationship of affected family members revealed that the most frequently affected relatives were those who had the closest relationship with the children with duodenal ulcers. 19 of 23 children had one or other parents or sib affected with the disease. In 13 children there was a family history of peptic ulcer in the father.

Discussion

Our findings show a significant familial aggregation of peptic ulcers and emphasize the importance